REMARKS

Claims 3, 6, 7, 11, 12 and 13 have been amended. The amendments add no new matter to the claims. Claim 22 has been added. Support for this claim can be found in the specification, e.g., on Page 4, lines 29-30, Page 5, lines 8-10, and in the Examples, beginning on Page 12. Claims 23-24 have also been added; support for these claims can be found throughout the specification, including the examples, beginning on Page 12. Claim 2 has been cancelled. Claims 5 and 15-21 have been withdrawn in response to the restriction requirement dated June 17, 2003.

Claim Objection

The Examiner has objected to Claim 1 because the terms "IFN" and "IFNAR2c" are not spelled out at the first occurrence of the terms. Claim 1 has been amended such that the terms are now spelled out. Applicants respectfully request withdrawal of the Examiner's objection.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner has rejected Claims 1-4 and 6-14 under 35 U.S.C. §112, first paragraph, for not being enabling for the invention as claimed.

The Examiner has indicated that the Specification does not reasonably provide enablement for a method of "potentiating any effects of a type I IFN" on target cells by "any route of delivery". More specifically, it has been indicated that it would require undue experimentation to make and/or use the invention as claimed based on

1. The fact that Applicants have not demonstrated the ability of increasing IFNAR2c receptor to potentiate "any effects" of a type I IFN on cells;
2. The question of the route of delivery, which the Examiner characterizes as being "by any route of delivery" (see Office Action, pg 4);

3. That a preferred route of delivery (see Claim 10), the use of viral-based gene therapy to deliver a gene encoding IFNAR2c to a target cell, would have been unpredictable, because viral gene therapy is an unpredictable art; and
4. That Applicants have not provided a working example of *in vivo* delivery of the IFNAR2c gene.

As regards item 1 above, Applicants have amended Claim 1 to now read "A method of potentiating the anti-growth effects of a type I interferon". Applicants believe that the Specification provides sufficient grounds for enablement of the anti-growth effects claimed in modified Claim 1, and assume that the Examiner agrees as well, based on the remarks on page 3 of the Office Action dated February 11, 2004.

In response to item 2, it is urged that the introduction of a gene into a cell was routine and conventional on the date the application was filed. For example, the Specification (e.g., pg 7, line 27 to pg 8, line 7) discloses numerous methods of introducing DNA into cells, such as vector-assisted delivery, use of liposomes, or poly-lysine conjugates. No evidence has been provided that gene transfection technology is anything more than routine, and it is unclear what aspect would require any additional, let alone "undue," experimentation. Nonetheless, Applicant has added Claim 22 which is further comprising introducing an exogenous polynucleotide encoding the IFNAR2c polypeptide into cells in culture to form said modified cells. See, also Claim 4.

As regards Items 3 and 4, it is argued in the Office action that the field of viral gene therapy is sufficiently unpredictable that it would require undo experimentation for one skilled in the art to make and use the claimed method, absent Applicants' providing an *in vivo* example. The Examiner cites several reviews, dating back to 1997, which discuss the problems which must be dealt with when designing viral gene therapy.

Contrary to the statements in the Office action, *in vivo* gene therapy has had success, perhaps not at the levels that might make it suitable for commercial use or to meet FDA approval. However, neither commercial success or FDA approval are relevant to satisfy the statutory requirements. In particular, the MPEP §2107.01 clearly states: "If

an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on a lack of utility is not appropriate. See In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995); In re Gardner, 475 F.2d 1389, 177 USPQ 396 (CCPA), reh'g denied, 480 F.2d 879 (CCPA 1973); In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1971)." It is bedrock law that an applicant does not have to demonstrate that a claimed compound is fully effective or that it meets efficacy and safety requirements in humans. See, generally, M.P.E.P. §2107.01 II, III. It appears that the examiner has confused FDA approval with therapeutic use for the purposes of patentability. See, M.P.E.P. §2107.03, V.

In fact, success has been achieved with gene therapy. For instance, studies by Tada et al. (*J. Clin Invest.* 108:83-95) and Cao et al. (*Cancer Gene Therapy* 8:497-505, 2001) demonstrate the utility of gene therapy with IFNβ. Success has also been reported for SCID and other immune system diseases. Accordingly, one skilled in the art would reasonably conclude that transfection of cells with the INFAR2c gene *in vivo* would be effective in the treatment of disease related to uncontrolled or abnormal growth.

The Examiner cites several references (U.S. Patents 5,681,558; 5,821,078, and 6,569,420) to show that at the filing date "little was known on the use of an exogenous gene encoding IFNAR2c polypeptide for potentiating any effect of a type I IFN on any target cell". Applicants have therefore increased the knowledge base in this field as the instant Specification shows that transfection of cells with the INFAR2c gene produces cells which have increased levels of INFAR2c, and that the anti-growth effects of a type I IFN are potentiated in such transfected cells.

The PTO has indicated that *in vivo* data is not unnecessary. See, e.g., *In re Brana,* 51 F .3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). Applicants have clearly demonstrated the success of the claimed approach in cells, and that information is adequate to establish the patentability of the full scope of the claims.

Applicants respectfully request that the Examiner reconsider the rejection of Claims 1-4 and 6-14 under Section 112, first paragraph, and withdraw the rejection.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected Claim 11 under 35 U.S.C. §112, second paragraph, for being indefinite. The Examiner has indicated that the term "derived from" is unclear. As per the Examiner's suggestion, Claim 11 has been amended to recite "the viral vector is a retroviral or adenoviral vector".

Applicants believe that the amendment to Claim 11 addresses the Examiner's rejection and respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. §102 (b)

The Examiner has rejected Claims 1-4, 6 and 12-13 under 35 U.S.C. §102 (b) as being anticipated by Domanski et al. (*J. Biol. Chem.* 273:3144-3147, 1998).

For a reference to inherently anticipate a claimed invention, the allegedly inherent characteristic must necessarily flow from the teachings of the prior art. See, e.g., Schering Corp. v Geneva Pharmaceuticals, 67 USPQ2d 1664 (Fed. Cir. 2003); Ex part Levy, 17 USPQ2d 1461 (BPAI 1990). The result must inevitable and happen each time.

This is not the case for the cited references. For example, enclosed are several articles which show that antiproliferative and antiviral activities of IFN are not "inherently" linked (de la Maza et al., *Infect. Immun.* 47:719-722 (1985); Khine and Lingwood, *J. Cell Physiol.* 182:97-108 (2000); and Fish et al., BBRC 112:537-546 (1983)), and that therefore, the anti-vrial effects reported in Domanski et al. do not necessarily and inevitably lead to anti-growth effects.

In addition, the experiments in the Domanski et al. reference show effects of human type I IFN on mouse cells which contain both endogenous mouse IFN receptor subunits and human IFN receptor subunits which have been transfected into the mouse cells. There is, therefore, the likelihood that the anti-viral induction shown in Table 1 reflect not just the interaction of human IFN with human IFN receptor subunits, but also with mouse IFN receptor subunits as well, and it is obvious that this mixed system does

not provide clear data as to what interactions are being measured. See, also Claims 23 and 24 which recite "human."

Furthermore, the cited reference does not show "increasing the number of functional IFNAR2c receptor chains ..." The cells lines described in Domanski et al. are not treated at any time during the experiment to increase the number of receptors. If a reference fails to teach every element of a claim, it can not anticipate it.
Applicants believe that in light of the amendment to Claim 1 and the arguments presented above, the rejection of Claims 1-4, 6 and 12-13 should be withdrawn and respectfully request their withdrawal by the Examiner.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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